TOGA anchor primer sequence has an extra "C" nucleotide (underlined) in the *Not*I site (bolded sequence) of the primer that destroys the *Not*I site. Given that the anchor primer is described in the specification as having a *Not*I site (page 57, lines 4-7), one of ordinary skill would recognize that the TOGA primer sequence was an obvious error due to the absence of a *Not*I site, and would further realize that deletion of a "C" would provide a correct *Not*I site. Furthermore, the TOGA anchor primer is correctly listed in the specification on page 56, lines 21-22.

Finally, please replace the originally-filed abstract page 120 with the attached substitute sheet 121. The substitute sheet merely changes the page number from 120 to 121 and contains the same abstract as originally filed.

The Amendment to the Claims

Please delete the 54 claims as originally filed and replace them with the 11 sheets of new claims 1-91 (copy attached). The new claims find support generally in the description and claims as originally filed, and in particular, new claims 76-91 find support in Table 2 (pages 92-93) of the specification. Accordingly, new claims 1-91 add no new matter.

Reasoned Statement Regarding Novelty (PCT Article 33(2))

Claims 1-6 are alleged to lack novelty. The Written Opinion alleges that due to the lack of an indication of fragment length or the origin or specificity of the polynucleotide in claim 1, any prior art polynucleotide fragment will take away novelty of claims 1-6.

Claim 1 has been amended to recite an isolated nucleic acid molecule comprising a polynucleotide chosen from the group consisting of SEQ ID NO:1

through SEQ ID NO:25. Claim 2 has been amended to recite an isolated polypeptide encoded by a polynucleotide chosen from the group consisting of SEQ ID NO:1 through SEQ ID NO:25. Claims 3 and 4 depend from claim 1, and claims 5 and 6 depend from claim 2. In contrast to the allegation in the Written Opinion, the sequence and length of the polynucleotide of claim 1 (i.e., a polynucleotide chosen from SEQ ID NOS 1-25) are clearly indicated in the Sequence Listing. Further, the specification indicates that the polynucleotide of claim 1 and the corresponding polypeptide of claim 2 originate from neonatal mouse brain (see, for example, specification at page 54, lines 15-24). In addition, the specificity of the polynucleotide of claim 1 and polypeptide of claim 2 is provided in Table 2 (wherein the polynucleotide sequence is identified and further described in terms of homology to Gen Bank sequences) and Examples 1-10 (wherein further characterization of the polynucleotide is provided).

D1 reports the differential expression of six cDNAs during LPS-activation of microglia cells. Although the D1 reference reports that the six cDNAs correspond to the 3' end of the mRNAs (page 102, paragraph 2 of column 2), it does not disclose the nucleotide sequence of any of the cDNAs. Moreover, D1 offers no further description for four of the six cDNAs. Of the remaining two cDNAs, D1 reports that they are serine proteinase inhibitors that share homology (69%) with bases 1609-1707 of human squamous cell carcinoma antigen cDNA (accession no. S66896). As indicated in Table 2, none of the polynucleotides of claim 1 share homology with this sequence (see Table 2). Accordingly, D1 does not teach a nucleic acid comprising a polynucleotide of claim 1 or a polypeptide encoded by a polynucleotide of claim 1 (claim 2).

D2 reports that the *mu* opioid receptor (MOR) is constitutively expressed in microglia and macrophages and provides the cDNA sequence of MOR from human brain (Gen Bank accession number L29301). In contrast, the present invention is directed to polynucleotides and their encoded polypeptides that are differentially regulated in microglia versus macrophages, or differentially regulated in activated microglia and/or activated macrophages. Further, as indicated in Table 2, none of the polynucleotides of claim 1 share homology with the MOR cDNA (see Table 2). Accordingly, D2 does not teach any of the polynucleotides or polypeptides of claim 1 or claim 2.

D4 provides the rat, mouse, and human cDNA sequence of the CC chemokine receptor CKR5. As indicated in Table 2, none of the polynucleotides of claim 1 share homology with the CC chemokine receptor CKR5 cDNA (see Table 2). Accordingly, D4 does not teach any of the polynucleotides or polypeptides of claim 1 or claim 2.

In addition, the Written Opinion alleges that claims 7-10, 17, 18, 29, and 30 also lack novelty because recombinant vectors and methods for producing the same (claims 7-10), treatment and diagnostic methods (claims 17 and 18), and kits and methods for detecting the presence of genes (claims 29 and 30) are known in the art. However, as discussed above, the polynucleotide recited in new claim 1 and the corresponding polypeptide recited in new claim 2 are indeed novel. Therefore, claims reciting the introduction of the novel polynucleotide or fragments thereof into vectors or host cells, the administration of the polynucleotide or polypeptide to treat or diagnose a susceptibility to a medical condition, such as a neuroinflammatory or neurodegenerative disease, or the use of the polynucleotide or fragments thereof for detection purposes are indeed novel.

Statement regarding PCT Rule 5.1(a)(ii)

The specification has been amended to identify D1-D4 and include the relevant background art disclosed in the documents D1-D4.

Statement Regarding Clarity (PCT Article 6)

The Written Opinion observed that claim 1 lacked clarity because the subject matter allegedly covers a large amount of possible definitions of the claimed nucleic acid, ranging from fragments of the given sequences to encoding sequences for polypeptide epitopes, variants, and allelic variants, and species homologues of translation products. This observation is moot in view of the amended claims. Claim 1 has been amended such that the subject matter is covered in new claims 4, 6, 7 and 9. Claim 4 recites an isolated nucleic acid molecule at least ten bases in length that is hybridizable to the isolated nucleic acid molecule of claim 1 under stringent conditions. Stringent hybridization conditions are clearly defined on page 12, lines 8-12. Accordingly, the possible nucleic acid compounds are clearly defined as those nucleic acid compounds of particular length and sequence to hybridize under specified conditions to a defined sequence.

Claim 6 recites an isolated nucleic acid molecule encoding a fragment of the polypeptide of claim 2. Polynucleotide fragments are clearly defined on page 22, lines 17-31. Polypeptide fragments are clearly defined on page 22, line 33 to page 23, line 6. Accordingly, the polypeptide fragments of the instant invention are clearly defined.

Claim 7 recites an isolated nucleic acid molecule encoding a polypeptide epitope of the polypeptide of claim 2. Polypeptide epitopes are defined on page 23.

line 32 to page 24, line 14. In view of the definitions provided, the nucleic acid compounds of the instant invention are clearly defined.

Claim 9 recites an isolated nucleic acid encoding a species homologue of the polypeptide of claim 2. Species homologues are defined on page 15, lines 18-20. In view of the definitions provided, the nucleic acid compounds of the instant invention are clearly defined.

In addition, the Examiner has objected to claim 8 for failure to contain a single method step. This claim has been amended (see new claim 13), rendering the rejection moot.

The Office also alleges that the vague statement on page 81 lines 5-7 implies that the subject matter may be different from that which protection is sought. The specification has been amended to delete lines 5-7, thereby rendering the observation moot.

Respectfully submitted,

Date: December 18, 2000

By: _____
Anita J. Terpstra
U.S. Reg. No. 47,132